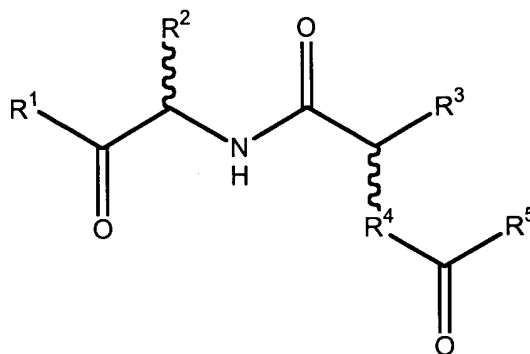


AMENDMENT TO THE CLAIMS

Claim 1 (currently amended): A chemical compound comprising an analog or a derivative of (S,S,R)-(-)-actinonin having the structure:



wherein R¹ is an optionally substituted or halogenated, ~~indoline indole, pyrrole, or imidazole alkyl, aryl, heteroalkyl or heteroaryl amine, said R¹ further comprising a cyclic or bicyclic structure;~~

R² is methyl, CH₂CH₃, (CH₂)₂CH₃, C(CH₃)₃, phenyl, 3,4-dichlorophenyl, biphenyl, benzyl, 4-hydroxybenzyl, piperidine, N-Boc-4-piperidine, CH₂-(N-Boc-4-piperidine), 4-tetrahydropyran, CH₂-4-tetrahydropyran, 3-methyl indolyl, 2-naphthyl, 3-pyridyl, 4-pyridyl, 3-thienyl;

R³ is R² or C₃₋₈alkyl,

R⁴ is C₁₋₃alkyl; and

R⁵ is NH₂, OH, NHOH, NHOCH₃, N(CH₃)OH, N(CH₃)OCH₃, NHCH₂CH₃, NH(CH₂CH₃), NHCH₂(2,4-(OCH₃)₂Ph), NHCH₂(4-NO₂)Ph, NHN(CH₃)₂, proline, or 2-hydroxymethyl pyrrolidine.

Claim 2 (currently amended): The chemical compound of claim 1 wherein:

~~R¹ is NHCH₂Ph, NHCH₃, NHCH₂CH₃, N(CH₃)₂, N(CH₂CH₃)₂, NHCH₂(2,4-(OCH₃)₂Ph), NHCH₂(4-NO₂Ph), hexamethyleneamine, methyl-2- or 3-hexamethyleneamine-carboxylate, heptamethyleneamine, pyrrole, indole, aziradine, imidazole, 1,4-dioxan-2-yl-methylamine, 3,4-dihydro-2H-1,4-benzoxazin-6-ol, 6-methoxy-1,2,3,4-tetrahydro-isoquinoline, piperazin-1-yl-pyridin-3-yl-methanone or further comprising:~~

~~proline optionally substituted to independently form a methyl, ethyl, benzyl or t-butyl ester;~~

~~azetidine optionally substituted with one of 2- or 3-methyl or ethyl or a methyl-, ethyl- or benzyl-2- or 3-carboxylate;~~

~~indoline is optionally substituted with one of a C2-C7 fluoro or methyl-2-carboxylate;~~

~~pyrrolidine optionally substituted with 2-methylamino, 2-hydroxycarbamoyl, one of 2- or 3-hydroxymethyl, one of 2- or 3-~~

~~methyl, ethyl, benzyl or phenyl, one of 2,3-, 2,4-, or 2,5-dimethyl, 2,5-diethyl, one of methyl-, ethyl-, t-butyl- or benzyl-3- carboxylate, or methyl-(2-methyl-5- carboxylate);~~

~~piperidine optionally substituted with 2- or 3-methyl- or ethyl, one of methyl-, ethyl-, or benzyl- 2-, 3-, 4- carboxylate;~~

~~morpholine optionally substituted with one of methyl-, ethyl-, or benzyl- 2- or 3- carboxylate; or~~

~~piperazine optionally substituted with 1-benzyl, N-t-boc, 1-furfuryl, 1-isonicotinoyl, or one of pyridin-2-, 3- or 4-ylmethyl;~~

~~or pharmaceutically acceptable salts or hydrates thereof.~~

Claim 3 (canceled).

Claim 4 (currently amended): A pharmaceutical composition [[,]] comprising, a therapeutically effective amount of the compound of claim 1 and a pharmaceutically acceptable carrier.

Claim 5 (currently amended): A method for asymmetrically synthesizing a chemical compound having the structure of claim 1, ~~said structure further comprising (S,S,R)-(-)-actinonin, said method~~ comprising the steps of:

- a) forming an optionally *O*-protected R^1 -1-carbonyl-C2-(R^2)-methylethylamine from R^1 and an *N*-protected R^2 -amino acid 2,5-dioxo-pyrrolidinyl ester and deprotecting said *N*-protected R^2 -amino acid with a suitable agent comprising trifluoroacetic acid;
- b) forming an R^3 -carbonyl-oxazolidone from 4-isopropyl-oxazolidin-2-one and R^3 -carbonyl chloride;
- c) treating a solution of 4-(*S*)-isopropyl-oxazolidin-2-one with a solution of a base comprising *n*-butyl lithium in hexanes and adding an R^3 -carbonyl chloride thereby forming an R^3 -carbonyl oxazolidinone;
- d) treating a solution of the R^3 -carbonyl oxazolidinone sequentially with a base comprising lithium diisopropylamide and with a bromo- R^4 acid-*tert*-butyl ester thereby forming an oxazolidine- R^3 -carbonyl- R^4 -acid *tert*-butyl ester;
- e) treating a mixture of the an oxazolidine- R^3 -carbonyl- R^4 -acid *tert*-butyl ester in tetrahydrofuran and water sequentially with hydrogen peroxide in water and with lithium hydroxide in water thereby forming a C2(R^3)- R^4 -dicarboxylic acid *tert*-butyl ester;
- f) treating a mixture of the C2(R^3)- R^4 -dicarboxylic acid 4-*tert*-butyl ester and hydroxysuccinimide in a solvent

comprising dioxane or dimethylformamide with an imide comprising dicyclohexylcarbodiimide thereby forming an C2(R³)-R⁴-dicarboxylic acid *tert*-butyl ester-(2,5-dioxo-pyrrolidin-1-yl) ester.

g) treating a solution of said optionally *O*-protected R¹-1-carbonyl-2-(R²)-methyleneamine in a solvent comprising tetrahydrofuran sequentially with triethylamine and with the C2(R³)-R⁴-dicarboxylic acid *tert*-butyl ester-(2,5-dioxo-pyrrolidin-1-yl) ester thereby forming an optionally *O*-protected R¹-1-carbonyl-2-(R²)-carbamoyl-methylene(R³)-R⁴-carboxylic acid *tert*-butyl ester;

h) treating a solution of said optionally *O*-protected R¹-1-carbonyl-C2(R²)-carbamoyl-methylene(R³)-R⁴-carboxylic acid *tert*-butyl ester in a solvent comprising methylene chloride with trifluoroacetic acid thereby forming an optionally *O*-protected R¹-1-carbonyl-C2(R²)-carbamoyl-methylene(R³)-R⁴-carboxylic acid;

i) treating said optionally *O*-protected R¹-1-carbonyl-2-(R²)-carbamoyl-methylene(R³)-R⁴-carboxylic acid and hydroxysuccinamide with an imide comprising dicyclohexylcarbodiimide thereby forming a optionally *O*-protected R¹-1-carbonyl-C2(R²)-carbamoyl-methylene(R³)-R⁴-carboxylic acid 2,5-dioxo-pyrrolidin-1-yl ester;

j) treating a suspension of R⁵ or the chloride thereof, said R⁵ optionally O-protected, in a solvent comprising dimethylformamide sequentially with triethylamine and with a solution of said O-protected R¹-1-carbonyl-C2(R²)-carbamoyl-methylene(R³)-R⁴-carboxylic acid 2,5-dioxo-pyrrolidin-1-yl ester in a solvent comprising dimethylformamide thereby forming an R¹-1-carbonyl-C2(R²)-carbamoyl-methylene(R³)-R⁴-carbonyl-R⁵, said R¹ and R⁵ independently optionally O-protected; and

k) hydrogenating said R¹ and R⁵, said R¹ and R⁵ independently comprising an O-protecting group, with hydrogen gas and a catalyst comprising palladium hydroxide in activated carbon wherein ~~(S,S,R)-(-)-actinonin~~ or said chemical compound of claim 1 is thereby formed.

Claims 6-9 (canceled).

Claim 10 (original): A method for the treatment of a neoplastic disease comprising the step of administering to an individual in need of such treatment a pharmacologically effective dose of the chemical compound of claim 1.

Claim 11 (canceled).

Claim 12 (original): The method of claim 10, wherein said individual is a human or an animal.

Claim 13 (original): The method of claim 10, wherein said neoplastic disease is selected from the group consisting of human ovarian carcinoma, prostate carcinoma, mammary carcinoma, head and neck squamous cell carcinoma, non-small-cell-lung-cancer adenocarcinoma, non-small-cell-lung-cancer squamous cells, and acute myelogenous leukemia.

Claim 14 (currently amended)

A method of inhibiting the growth of a tumor cell *in vitro* comprising the step of contacting said cell with a pharmacologically effective dose of the chemical composition of claim 1.

Claim 15 (canceled).

Claim 16 (original): The method of claim 14, wherein said tumor cell is selected from the group consisting of human

ovarian cancer cells, prostate cancer cells, mammary cancer cells, head and neck squamous cancer cells, non-small-cell-lung-cancer cells, adenocarcinoma cells, non-small-cell-lung-cancer squamous cells, and acute myelogenous leukemic cells.

Claims 17-21 (canceled).